

**Ngozi Ekeke¹, Elias Aniwada², Joseph Chukwu¹, Charles Nwafor¹, Anthony Meka¹,
Chukwuka Alphonsus¹, Okechukwu Ezeakile¹, Adeyemi Ajayi³, Festus Soyinka⁴, Francis Bakpa⁵,
Victoria Uwanuruochi⁶, Ezechukwu Aniekwensi⁷, Chinwe Eze¹**

¹German Leprosy and TB Relief Association, Nigeria

²University of Nigeria Teaching Hospital, Enugu, Nigeria

³Sacred Heart Hospital, Abeokuta, Nigeria

⁴Ogun State Ministry of Health, Abeokuta, Nigeria

⁵Delta State Ministry of Health, Nigeria

⁶Federal Medical Centre, Umuahia, Nigeria

⁷Federal Medical Centre, Asaba, Nigeria

Screening diabetes mellitus patients for tuberculosis in Southern Nigeria: A pilot study

Abstract

Introduction: Diabetes mellitus (DM) and tuberculosis (TB) are of great public health importance globally, especially in Sub-Saharan Africa. Tuberculosis is the third cause of death among subjects with non-communicable diseases. DM increases risk of progressing from latent to active tuberculosis. The study aimed to ascertain yield of TB cases and the number needed to screen (NNS) among DM patients.

Material and methods: A cross-sectional study was conducted at 10 health facilities with high DM patient load and readily accessible DOTS center in 6 states of southern region of Nigeria over a period of 6 months under routine programme conditions. All patients who gave consent were included in the study. Yield and NNS were calculated using an appropriate formula.

Results: 3 457 patients were screened with a mean age (SD) of 59.9 (12.9) years. The majority were male, 2 277 (65.9%). Overall prevalence of TB was 0.8% (800 per 100 000). Sixteen (0.5%) were known TB cases (old cases). There were 221 presumptive cases (6.4%) out of which 184 (83.3%) were sent for Xpert MTB/Rif assay. Eleven (0.3%) new cases of TB were detected, giving additional yield of 40.7% and the number needed to screen (NNS) of 315. All the 11 patients were placed on anti-TB treatment.

Conclusions: The prevalence of TB among DM patients was higher than in the general population. The yield was also good and comparable to other findings. This underscores the need for institute active screening for TB among DM patients. Further studies are recommended to identify associated factors to guide policy makers in planning and development of TB-DM integrated services.

Key words: diabetes, tuberculosis, screening, yield, number needed to be screened, Nigeria

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Introduction

Diabetes mellitus (DM) and tuberculosis (TB) are major lethal diseases of great public health importance globally [1]. This is the most visible in Sub-Saharan Africa (SSA) due to the converging epidemics of both communicable and non-communicable diseases. The World Health Organization (WHO) has identified DM as a global epidemic. The relationship between diabetes and

tuberculosis as well as their synergistic role in causing human disease may be the next challenge for global tuberculosis control [2].

Diabetes prevalence is increasing globally, especially in low- and middle-income countries due to ageing, population growth, rapid economic, social, and lifestyle changes [3, 4]. About 422 million people worldwide were living with diabetes in 2014 [5]. The global prevalence of diabetes was estimated to be 8.5% among adults

Address for correspondence: Elias Aniwada, Department of Community Medicine, University of Nigeria Teaching Hospital, Enugu, Enugu State, Nigeria; e-mail: eaniwada@gmail.com
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aged 18 years and above [5]. In 2012, diabetes was the direct cause of 1.5 million deaths [5]. Eighty percent (80%) of these people live in low- and middle-income countries, including Nigeria where TB prevalence is equally high. This is also where 80% of all deaths due to DM occur [5]. About 10–15% of global TB cases are linked to diabetes [6]. Diabetes mellitus has recently emerged as risk factor for developing active TB [7]. Diabetes triples a person's risk of developing TB [8–11]. The global economic burden of diabetes is enormous. In Africa, the mean annual cost for diabetes care ranges between \$2 144 and \$11 430 (direct costs \$876–1 220) [12].

Tuberculosis ranks as the second leading cause of death from an infectious disease globally next to the human immunodeficiency virus (HIV). DM and TB comorbidities complicate tuberculosis management and negatively influence its treatment outcome [13, 14]. In 2014, 9.6 million people fell ill with TB, 1.5 million died from TB and one in three individuals in the world was infected with latent TB [5]. The World Health Organization (WHO) reported that in 2017, globally there were estimated 10.0 million incident cases of TB (range, 9.0–11.1 million), which translates to 133 cases (range, 120–148) per 100 000 population. Most of these cases in 2017 occurred in Asia (44%) and the African Region (24%) [15]. In Nigeria, tuberculosis is still a grave public health problem. It is associated with huge economic burden just as in other low-income countries [16–18]. In Nigeria, despite the National TB and Leprosy Control Programme (NTBLCP) reporting 94 604 cases in 2012, this number only represents 51% of the cases estimated to have occurred in the country that year [19]. In 2017, the incidence of TB in Nigeria was 418 cases (range 273–594) [15].

The presence of DM alone does not justify screening or treatment of latent TB infection (LTBI). However, when combined with other risk factors for TB, the presence of DM may be sufficient to justify screening and treatment of LTBI, even in a low TB incidence setting [20]. The Sustainable Development Goals (SDGs) among other targets, made ending the global TB epidemic a priority. To achieve this, new strategies need to be employed. Passive case finding which used to be the norm whereby patients present themselves for TB screening seems not yielding desired result. Active case finding (ACF) is believed to contribute to the earlier detection of persons with TB. This will lead to early initiation of treatment, better therapy outcomes for individuals and ultimately, it will reduce transmission in the community [21–23].

The World Health Organization and the Union have launched a new 'Collaborative Framework for the care and control of Diabetes and Tuberculosis' with one of the most important activities being the routine implementation of bi-directional screening of the two diseases [24]. In Nigeria, there are no policies identifying DM patients with TB symptoms, or minimizing the time spent by patients with probable DM-TB co-morbidity in the diabetes clinics. In addition, evidence to inform the development of interventions to address the TB burden among DM patients is crucial but lacking. Moreover, the methods of screening, recording and reporting DM and TB co-morbidity in routine health care settings are not well determined, and these knowledge gaps need to be addressed. There is a need for relevant stakeholders, including: WHO, National TB and Leprosy Control Programme and government agencies/departments responsible for non-communicable diseases to review and discuss linkages between DM and TB — hence the need for bidirectional screening and the WHO Union Collaborative Framework. A multicenter, unidirectional study to assess the burden of diabetes mellitus among TB patients was recently completed in 6 selected states in southern Nigeria the results of which have been published [25]. The study seeks to address the second arm, i.e. intensified TB screening among patients with diabetes mellitus. The feasibility of the screening (DM patients for TB), burden and challenges will be evaluated within routine health care services to inform policy change and develop generic protocols for its implementation.

Screening persons with DM for TB could be one of the strategies for early and increased TB case detection in Nigeria. These informed the programme implementation of active case finding through screening to ascertain incidence, yield, number needed to screen (NNS) for a case of TB among DM patients.

Material and methods

Study area

The study was conducted in the southern region of Nigeria spanning through all the 3 geopolitical zones and involving 6 states (two from each geopolitical zone) namely; Ogun, Ondo, Edo, Delta, Enugu and Abia States. Diabetes clinics of selected health facilities with high DM patient load and readily accessible DOTS centre were selected in each state for the study. This region hosts the major oil producing

states. They engage in farming, fishing, mining, trading as well as civil/public services. There are well established health centres, including tertiary, secondary and primary facilities that care for patients, including those with DM and TB. However, 10 health clinics were used for the study. These were the major centres caring for both diseases in the states.

Study design, duration and population

A hospital-based cross-sectional study was done under programme implementation. The study was conducted over 8-month period from February to October 2018. All diagnosed cases of diabetes mellitus who were aged 15 years and above, registered with and attending Diabetes Clinics in selected health facilities within the study period and who gave informed consent were included.

Sampling technique and sample size determination

All diabetic clients attending DM clinics at the selected health facilities who met the inclusion criteria were included in the screening. They were recruited consecutively as they presented at clinic throughout the period of the study. A total of 3 457 patients were included in the study.

Procedure of screening

The subjects were DM patients aged 15 years and above who have been registered in the DM clinic for care. Presumptive and diagnosed TB cases were screened for HIV in line with the national TB guidelines. The screening for TB was carried out at each patient's visit (minimum of one month interval; however, each subject was reported only once during the project period) using a symptom-based standardised checklist.

Referral of identified presumptive TB cases (among DM patients) to TB clinic

Trained research assistants worked in collaboration with the staff at the DM clinics to: conduct a symptomatic TB screening for all eligible DM patients using appropriate tools (checklist), identify presumptive TB cases among those screened for TB; collect 2 sputum specimens from identified presumptive TB cases; send sputum specimens for GeneXpert diagnosis (second sputum specimen was equally processed if the first was negative), refer all diagnosed TB cases to TB clinic for treatment and record necessary data using tools. Good cooperation and collaboration were established between the 2 sets of

staff working in the different service areas (DM and TB clinics).

Data collection and analysis

Patient information was extracted from a standard globally used register and analysed. The records were filled by trained health workers to ensure good quality data. Double data entry was done to ensure accuracy. IBM Statistical Package for Social Sciences Version 21 was used for data entry, editing and analysis. Results were presented in tables. Yield $[(\text{new TB cases}/\text{total number with TB}) \times 100]$ and the number needed to screen (number of patients/new TB cases) were calculated. Mean, standard deviation, proportion and percentages were used as summary measures, where appropriate.

Ethical consideration

The Ethics and Research Advisory Committee of University of Nigeria Teaching Hospital (UNTH), Enugu approved the study. Approval was also obtained from the State TB Control Programme in six states selected for the project. Permission was equally obtained from heads of the facilities and written informed consent obtained from the patients. Confidentiality of data was ensured in course of the research.

Results

Table 1 shows that a higher proportion of patients were aged ≥ 60 years 2 669 (77.2%) and with their mean age 59.86 years. Males were higher in proportion 2 277 (65.9%). They were predominantly civil/public servants — 1 428 (41.3%) and traders — 1 308 (37.8%). The majority had BMI of 25–29.9 kg/m^2 1 340 (38.8%) followed by ≥ 30 kg/m^2 1 019 (29.5%). Only 22 (0.6%) currently smoked cigarettes or tobacco-based products. As well, only 3 (0.1%) tested positive for HIV. Most were type 2 DM 3 328 (96.3%).

Table 2 shows that 6 386 patients attended the clinic within the 6 months of the study. Of this number, 3 457 (54.1%) were new patients or attended the clinic once. These were the patients further studies were based on. Presumptive cases were 221 (6.4%) out of which 184 (83.3%) were sent for Gene Xpert. In all 11 (0.3%) tested positive following screening (new cases), 16 (0.5%) were known cases (old cases), and 27 (0.8%) had TB (old and new cases) among the patients studied. Among the 11 subjects that were newly detected, all were sent for treatment.

Table 3 shows that of the 3 457 patients studied, yield was 40.7% and the number needed to

Table 1. Characteristics of patients

Variables	Frequency (n = 3457)	Percent (%)
Age (years)		
< 60	788	22.8
≥ 60	2669	77.2
Mean (SD)	59.86 (12.86)	
Gender		
Male	2277	65.9
Female	1180	34.1
Occupation		
Civil/public servant	1428	41.3
Trading/business	1309	37.9
Others	722	20.9
BMI		
< 18.5	102	3.0
18.5–24.9	996	28.7
25–29.9	1340	38.8
≥ 30	1019	29.5
Current smoker		
Yes	22	0.6
No	3435	99.4
Type of DM		
1	129	3.7
2	3328	96.3
HIV		
Negative	3454	99.9
Positive	3	0.1

BMI — body mass index; DM — diabetes mellitus; HIV — human immunodeficiency virus

screen (NNS) for the yield was 315 patients. When disaggregated by characteristics, those aged < 60 years had yield of 42.9% and NNS of 263, males had yield of 50.0% and NNS of 326, civil/public servants had yield of 37.5% and NNS of 476, those with BMI of < 18.5 had yield of 60.0% and NNS of 34, smokers had yield of 47.8% and NNS of 313, type 2 DM patients had yield of 55.6% and NNS of 333 and those that were negative for HIV had yield of 38.5% and NNS of 345.

Discussion

The study reported that 11 DM patients or 0.3% of them tested positive following screening (new cases). More findings were that yield of TB cases was 40.7% and the number needed to screen to make diagnosis of a TB case was 315 DM patients. This is revealing and encouraging as these identified cases would have been the foci of spread among unsuspecting public with their consequent effects. The findings can partly be explained by the large population size involved in the study. It also gave credence to innovations aimed at controlling the menace of the diseases. For instance, the Collaborative Framework for the Care and Control of Diabetes and Tuberculosis as launched by WHO and the Union have routine implementation of bi-directional screening of the DM and TB as one of the important activities for control of TB [24]. In Nigeria where the methods of screening, recording and reporting DM and TB co-morbidity in routine health care settings are not well determined, these existing gaps can be addressed by such

Table 2. Distribution of patients studied

Variables	Formula*	Value
A. Total number of DM patient visits over 6 months (including revisit)		6386
B. Number (%) of new DM patients studied (excluding revisit)	$[(B/A) \times 100]$	3457 (54.1)
C. Number (%) of presumptive TB cases identified	$[(C/B) \times 100]$	221 (6.4)
D. Number (%) sent for GeneXpert test	$[(D/C) \times 100]$	184 (83.3)
E. Number (%) that with MTB detected (new cases)	$[(E/B) \times 100]$	11 (0.3)
F. Number placed on TB treatment		11
G. Number (%) of previously diagnosed (known) TB cases		16 (0.5)
H. Total number (%) of TB cases	$[(E+G)]$	27 (0.8)

*What was computed to get value

DM — diabetes mellitus; TB — tuberculosis; MTB — Mycobacterium tuberculosis

Table 3. Distribution of patients yield and number needed to screen disaggregated by patient characteristics

Variables	Number of patients	Total number with TB	Known TB cases	New TB cases	Yield (%)	NNS
	[A]	[B]		[C]	[(C/B)×100]	[A/C]
Overall	3457	27	16	11	40.7	315
Age (years)						
< 60	788	7	4	3	42.9	263
≥ 60	2669	20	12	8	40.0	334
Gender						
Female	1180	13	9	4	30.8	295
Male	2277	14	7	7	50.0	326
Occupation						
Civil/public servant	1426	8	5	3	37.5	476
Trading/business	1309	13	9	4	30.8	328
Others	722	6	2	4	66.7	181
BMI						
< 18.5	102	5	2	3	60.0	34
18.5–24.9	996	10	5	5	50.0	193
25–29.9	1340	6	4	2	30.3	670
≥ 30	1019	4	3	1	25.0	1019
Current smoker						
No	22	4	4	0	0.0	—
Yes	3435	23	12	11	47.8	313
DM type (n)						
1	129	3	3	0	0	—
2	3328	18	8	10	55.6	333
HIV status						
Negative	3454	26	16	10	38.5	345
Positive	3	0	0	0	0	—

BMI — body mass index; DM — diabetes mellitus; NNS — number needed to screen; HIV — human immunodeficiency virus; TB — tuberculosis

activities like this programme implementation screening exercise.

Above all, diagnosis of TB disease is the entry point in the management of TB cases. Consequently, early diagnosis through screening will lead to prompt commencement of chemotherapy; reduced transmission of the disease to unsuspecting populace they come in contact with and ultimately, a positive impact on the control of the disease in the general population.

Other previous studies supported findings from this study. In Taiwan, a screening done for pulmonary tuberculosis among the elderly with type 2 diabetes involving 3 087 patients detected 7 (0.2%) patients who were positive for pulmonary tuberculosis [26]. Similarly, in a symptom screening project in a tertiary care hospital in

south India, 12 cases were newly diagnosed of TB among 125 subjects that underwent TB investigation [27]. Another symptom screening research in Mexico detected 38 TB cases in 7 763 diabetes patients [28]. In China, TB was diagnosed in 14 of 4 085 patients with DM following active screening [29, 30]. Findings from previous studies have shown that screening for active TB among diabetics could improve case detection just like in other populations susceptible to TB, including HIV-infected individuals, gold miners, and prisoners in developing countries [31].

The number of diabetics needed to screen to find one extra case of TB is directly related to the TB prevalence among that population. For instance, in areas with TB prevalence less than 25 per 100 000 persons, at least 1 000 diabetic

individuals have to be screened to find one extra case of TB. With increasing prevalence, the number needed to screen to find one additional case of TB ranges from 4 to 442. This implies that the yield of screening increases with the prevalence of TB in that region [31]. Also, the population attributed risk for TB from DM is dependent upon DM prevalence as evidenced in studies which documented that in populations with a higher incidence of TB, DM is a more important risk factor [32]. DM accounts for a small proportion of TB cases in settings such as Australia with a low incidence of TB [33]. This number was 14.8% in India and 25% in a Mexican setting due to higher incidence and prevalence [34].

None of those that tested positive for HIV had TB. This is good as it would be disastrous for a patient to have two recognized major threats to TB diagnosis and treatment outcome. This may be explained by the age distribution of the studied DM patients. Most were aged > 60 years of which most HIV positive subjects may not live as long as that due to either the comorbidities, drug-drug interactions or opportunistic infections as both DM and HIV infection reduce immunity. Human immunodeficiency virus infection is considered as the most potent risk factor for TB. Nevertheless, the high prevalence of DM in the world and its effect on TB burden is greater than that of HIV infection [7]. Even though HIV has been documented to be the strongest risk factor for TB at an individual level, DM is seen as most important at the population level. This indicates that having both will carry far-reaching health and economic implications.

Conclusions

The number of positive cases identified following screening, yield of TB cases and the number needed to screen to make diagnosis of a TB case were encouraging. Active case finding in the form of screening as carried out in this study is needed to end the global TB. Such programme implementation should be encouraged and advanced to reduce scourge of TB and its co-morbidities.

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Conflict of interest

None declared.

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